

EXPERIMENTAL STUDY OF THE PLASTICOSTIMULATING EFFECT OF DRUGS BASED ON THE SYNTHETIC POLYMERS WHEN TOPICALLY APPLIED

V. M. Zubachyk, M. O. Iskiv, I. V. Gan, A. M. Yashchenko*

*Department of Therapeutic Dentistry (Head – D. M. Sci, Prof. V. M. Zubachyk); *Department of Histology, Cell biology and Embryology (Head – D. M. Sci., Prof. O. D. Lutsyk), Danylo Halytskyi National Medical University in Lviv. 79010, Ukraine, Lviv, Pekarska str., 69 B. E-mail: zubachyk@meduniv.lviv.ua*

ЕКСПЕРИМЕНТАЛЬНЕ ДОСЛІДЖЕННЯ ПЛАСТИКОСТИМУЛЮВАЛЬНОГО ЕФЕКТУ ПРЕПАРАТІВ НА ОСНОВІ СИНТЕТИЧНИХ ПОЛІМЕРІВ ПРИ МІСЦЕВОМУ ЗАСТОСУВАННІ

В. М. Зубачик, М. О. Іськів, І. В. Ган, А. М. Яценко

РЕЗЮМЕ

Експериментально на білих щурах встановлено, що препарати на основі синтетичних полімерів: органічного кремнію (силікін), поліамідного гелю (акваліфт), диметиламінометанолу (DMAE) при внутрішньослизозовому введенні у дозі 0,1 мл не викликають місцевих негативних реакцій у тварин. При морфологічному дослідженні виявлено рівномірне включення пластикостимуляторів у міжклітинний матрикс, їх здатність збільшувати кількість і активність фібробластів, сприяти ангиогенезу та трофіці тканин. Це зумовило формування сполучної тканини і спричинило потовщення субепітеліального шару слизової оболонки порожнини рота.

ЭКСПЕРИМЕНТАЛЬНОЕ ИССЛЕДОВАНИЕ ПЛАСТИКОСТИМУЛИРУЮЩЕГО ЭФФЕКТА ПРЕПАРАТОВ НА ОСНОВАНИИ СИНТЕТИЧЕСКИХ ПОЛИМЕРОВ ПРИ МЕСТНОМ ПРИМЕНЕНИИ

В. М. Зубачик, М. О. Иськов, И. В. Ган, А. М. Яценко

РЕЗЮМЕ

Експериментально на белых крысах показано, что препараты, содержащие синтетические полимеры: органический кремний (силикин), полиамидный гель (аквалифт), диметиламинметанол (DMAE) при внутрислизистом введении 0,1 мл не вызывают местных негативных реакций у животных. При морфологическом исследовании выявлено равномерное включение пластикостимуляторов в межклеточный матрикс, их свойство увеличивать количество и активность фибробластов, содействовать ангиогенезу и трофике тканей. Это обусловило формирование соединительной ткани и содействовало утолщению субэпителиального слоя слизистой оболочки полости рта.

Key words: *sylikin, aqualift, DMAE, oral mucosa, histomorphology.*

Aesthetic aspects are an integral part of the comprehensive concept of treating dental patients. It concerns not only the harmony in shape, size and color of teeth, but also the outline of lips and gums. Less attention is paid to the latter one, but the shape, contour, thickness, features of the gingival papillae cause the perception of the gums beauty [1, 3]. Therefore, the scientific rationale as to both the choice of medicine and best methods of their application for the removal of the aesthetic soft tissue defects through minimally invasive contouring were the subject of our experimental study.

The aim of the work was to analyze the histomorphological changes in the rats' mucous membrane after local application of the drug based on the compounds of the synthetic origin.

MATERIALS AND METHODS

The examination was carried out as an experiment on 30 white rats aged 9–10 weeks, weighing 210–230 gr. Interventions were performed under the general anaesthesia (0,5 ml of 4% solution of thiopental sodium into the peritoneum). Animals were injected intramuscularly with 0,1 ml of the studied medicine into the inside of the

cheek in the area near the molars close to the transition convolution of the alveolar process of the upper maxilla with the depth of the injection up to 2mm.

All animals were divided into 6 experimental groups of 5 animals each: the first group – intact animals served as a control, the second group – animals which were injected with placebo (saline); and the third group – animals which were injected intramuscularly with the drug based on the solution of organic silicon „Sylikin 1%” („ID-Farma”, Spain); the fourth group – animals injected with hydrogel „Aqualift” (JSC „National Center for Medical Technology”, Ukraine); the fifth group – animal injected with 2-demethylaminoethanol 4-ethanolacetaminobenzoat 6% – a synthetic medicine „DMAE” (OOO „Laboratory of Tuscany”, Russia).

The condition of the mucous membrane of the buccal cavity in each rat was determined due to the results of the visually-instrumental and histological studies. On the 30th day of the experiment, euthanasia of the rats was performed under the thiopental anaesthesia (20 mg/kg), in the injection site, areas of the mucous membrane together with the adjacent „healthy” areas of the tissue were carved. Samples of the tissue were fixed in the 10%

neutral formalin and embedded in paraffin. Paraffin sections with the thickness up to 7,5 mkm were produced on a rotary microtomes, stained with hematoxylin and eosin. Viewing and photography of the preparations were carried out using video system Nikon Eclips 200.

THE RESULTS AND DISCUSSION

Macroscopically, oral mucous membrane of the first control group is of pale pink colour, moist, with gleam and expressed tension without folds and visible damage. The results of the histological examination confirmed that the mucous membrane of the cheeks of the intact animals is covered with multilayered flat epithelium, in which a basal, spinous, granular and thin, oxyphilic-colored, horny layer is differentiated. Net plate of the mucous membrane is formed by loose connective tissue with a large number of cellular elements, among which fibroblasts dominate. It forms high papillae and smoothly develops into the submucosa containing bundles of collagen fibers, a large number of cellular elements and muscle fibers. Net plate and submucous base are well vascularized, in maxillary cheek area has finite secretory departments of the protein- mucous glands.

The animals of the second group after the single local injection of 0,1 ml of saline within a prolonged long period of observation, visible morphological changes in the local area of the drug use were not found. Mucous and submucous base had distinctive layered structure which was typical for the healthy animals of the control group. Thus, the intramucous placebo injection does not affect the morphological and functional condition of animals' mucosa. Therefore the results of the examination of the injectional usage of different, as to drugs may be compared and analytically considered.

In the third group of rats on the 30th day after the injection of a 1 %- sylikin into the buccal mucosa neither gel or their encapsulation or formation of cavities were not diagnosed. The obtained results testify bioinertness of the drug. The results of the histological studies showed, that the mucous membrane of the cheek has a typical structure similar to that of the previous animal group after the injection of the organic silicon. It is formed by the epithelial plate, represented by a stratified epithelium with signs of keratinization. In the epithelial plate, a basal layer is clearly differentiated (1 row of highly prismatic cells), spinous layer is formed by 10 rows polygonal-shape cells, among which are ones with signs of mitosis. Basal and lower rows of the spinous layer form the germinal (sprout) zone of the laminated epithelium. The granular layer – two rows of cells, in the cytoplasm of which there are basophilic colored granules of keratohyalin. In the granular layer oxyphilic colored thin stratum corneum lies. Net plate – loose connective tissue that contains a large number of cellular elements. Submucous base – the connective tissue that is characterized by a large number of thick bundles of collagen fibers, the muscle fibers are in the distal part, in the submucous

of the maxillary part of the cheek protein-and-mucous salivary glands are differentiated. Thus, the drug sylikin after a single injection for a long time does not cause significant changes in the oral mucosa of the animal. Taking into consideration the fact, that the organic silicon has a clearly marked defibrous effect, promotes the strength of collagen and elastin [2]; it proves to be useful as a medicine not for monotherapy but in combination with other drugs.

In the fourth group of animals, after the administration of the hydrophilic polyamide gel Aqualift, no clinical complications were found within the experiment. The drug does not move from the input zone, is not different in texture from soft tissues, is biocompatible, not allergic, does not cause an irritant effect and inflammatory reactions. It is histologically defined that, mucous membrane is covered with flat epithelium with keratinization and normal differentiation of the layers. Net plate does not almost form papillae. In some areas there are preserved papillary structures against the narrow subepithelial layer, areas with lower papillary structures and a doubled enlarged subepithelial layer due to proliferation of the epithelium. A great number of vessels, which are concentrated around the cellular elements of connective tissue and intensely painted oxyphilic collagen fibers can be determined. Thus, the drug Aqualift based on the synthetic polymers creates conditions under which the synthesis component of extracellular matrix improves. Branching of the vessels of the microvasculature that occurs under the influence of the drug, improves microcirculation, which enhances the synthetic and metabolic processes and have a positive impact on the tissue regeneration.

In the fifth group the drug DMAE is evenly distributed within the mucosa, is not rejected by the body after its administration. The bioinert allows administer it repeatedly into the one anatomic site. During the experiment mucous was not visually altered. After the DMAE application the mucous membrane is covered with stratified flat epithelium with keratinization and differentiation of normal layers. Net plate does not form papillae. Subepithelial layer is greatly thickened (its thickness is about twice bigger than the epithelial layer). In the submucous base between the bundles of collagen fibers, the number of primary amorphous substances and accumulation of adipocytes increases. A large number of vessels and oxyphilic collagen fibers is determined, blood vessels are dilated, filled with blood corpuscles, among which red blood cells predominate. Taking into consideration the mechanisms of action, DMAE may cause subclinical vasodilatation, transient swelling and accumulation of water in the hydrophilic structures of the subepithelial layer that is required to supply and maintain the function of the mucous membrane [4]. Minor accumulations of cellular elements around vessels, infiltration of the net plate and submucosal membrane with polymorphonuclear leukocytes (immune stimula-

tion processes) were observed. Thus, the DMAE drug affects not only the extracellular matrix, enhancing the processes of cell proliferation, but also as a stimulant acetylcholine receptor cells and endothelial sprout zone, causing activation of growth and differentiation of the cells. It is involved in the regulation of basic cellular functions [5], thereby changing the structure of intercellular space, the elasticity of the soft tissues increases and plastic stimulating effect is realized.

CONCLUSIONS

1. Macroscopically, on the 30th day of the experiment carried on rats, in the area of localization of drugs gel conglomerates or solution, their encapsulation or formation of cavities were not diagnosed, grafting materials are uniformly distributed evenly in the area of administration and didn't go beyond it. No signs of tissue aggression were not observed, drugs are bioinert which allows repeatedly typing them into the one anatomic site.

2. Microscopically, the formation of the connective-tissue capsule around the injected gel drug or the microcapsulation of its fragments were not discovered in the fragments of the mucous membrane of the cheek. Interstitial distribution and inclusion of means of remod-

eling into the extracellular matrix was observed, which caused the increased number and activity of fibroblasts, formation of bundles of collagen and other connective tissue components, and moreover improved angiogenesis and trophic of local tissues. As a result a significant thickening of the subepithelial layer and expressed plastic stimulation, occurred.

REFERENCES

1. Bekker U. et al. Minimal-invasive treatment of papillas defects in esthetic zone. / U. Bekker, I. Gabitov, M. Stepanov [et al.] // *Dentistry*.– 2011.– № 1 (151).– P. 14–19.
2. Porfenova I. A. Microelements in correction programs of esthetic face and body problems / I. A. Porfenova // *Mesotherapy*.– 2010.– № 11.– P. 38–46.
3. Rafiy C. Treatment possibilities in esthetic zone / C. Rafiy // *New in Dentistry*.– 2011.– № 2.– P. 6–27.
4. Smus V. V. Scientific investigations of DMAE in Cosmetology / V. V. Smus // *Mesotherapy*.– 2008.– Issue. 6–7, № 3–4.– P. 14–18.
5. Uhoda I. [et al.] Split face study on the cutaneous tensile effect of 2-dimethylaminoethanol (deanol) gel / I. Uhoda, N. Faska, C. Robert [et al.] // *Skin. Res. Technol.*– 2002.– Vol. 8, № 3.– P. 164–167.